

REMARKS

The preceding claim amendments and the following remarks are submitted as a full and complete response to the Office Action issued on September 27, 2007. Claims 1, 7, 17 and 20 have been amended to correct typographical errors that were indicated in the objections to claims 1, 7 and 20, or to define the claimed invention more clearly by addressing the rejection of claims 17 and 20 under 35 U.S.C. §112, second paragraph. No new matter has been introduced. Applicants respectfully submit that these claim amendments render both claim objections and the rejection for indefiniteness moot.

Applicants respectfully request entry of the claim amendments and favorable reconsideration of the application.

Rejection of Claims 18-20 under 35 U.S.C. §112, first paragraph

Claims 18-20 have been rejected for lack of written description, that is, for new matter. The Office argues that “[t]he originally filed specification and claims do not appear to contemplate a process of obtaining a solution containing a purified refolded biologically active monomeric bone morphogenetic factor, wherein said solution is free from oligomeric side products having the steps set forth in the claims.” Applicants respectfully traverse this rejection.

Each step of the process of claim 18 is fully supported by the original description of the instant application. See, e.g., page 5, second paragraph of the specification. Furthermore, the Examples described in the specification further supports the process

of claim 18. For example, it is described in the Examples that "[t]he steps (6) to (9) describe likewise the expression, direct refolding and purification in order to get **refolded monomeric MP52 with biological activity**". See page 12, last three lines from the bottom (emphasis added). Thus, the description for the steps (6)–(9) provides additional support for the process of claim 18.

With respect to support for the recitation of "solution is free from oligomeric side products," Applicants would like to direct the Office's attention to the disclosure regarding purification of monomeric MP52 after refolding, which appears on pages 16-17 of the specification. The step (8) describes three purification methods-ultrafiltration, isoelectric precipitation and semi-preparative reverse-phase chromatograph. After each purification process, purified monomeric MP52 was obtained as a solution. That is, the ultrafiltration was conducted through concentration and dilution processes, which resulted in a diluted solution containing purified monomeric MP52. After the isoelectric precipitation, the precipitate was dissolved in 0.2% phosphoric acid solution. The semi-preparative reverse-phase solution produced more purified monomeric MP52 in solution. In addition, oligomeric side products (possibly not correctly folded dimer) were removed during the purification steps. See page 16, last five lines from the first paragraph.¹

¹ The removal of the oligomeric side products is further confirmed by comparing Fig. 2 (showing the result of the refolding process) and Fig 3. (showing the result of the purification process after refolding). In figure 2, lane 2 shows oligomeric side products which is presumptively formed in addition to monomeric MP52 (MP52-A1a83) which is shown in lane 5. This oligomeric side product, however, is completely removed by the subsequent purification (ultrafiltration and isoelectric precipitation, lane 3 of Fig. 3 and

With respect to recitation of claim 19, "in which the cysteine responsible for dimer formation is deleted or substituted by another amino acid residue", as previously indicated with respect to claim 1, support can be found, for example, at pages 9-10, more particularly at page 9, lines 21-31.

As set forth above, Applicants respectfully submit that claims 18-20 as previously and currently amended are fully supported by the original specification of the present application. Accordingly, reconsideration and withdrawal of this new matter rejection are respectfully requested.

Rejection of Claims 1-8 and 16-20 under 35 U.S.C. § 103(a)

The Office has maintained the rejection of claims 1-8 and 16-20 under 35 U.S.C. §103 as obvious over Andou et al. (U.S. Patent No. 6,551,801) in view of Hötten et al. (U.S. Patent No. 6,972,321). Applicants respectfully traverse this rejection.

The previous Office Action proffered several options that Applicants can take to overcome this rejection. On further consideration, Applicants hereby submit a Declaration under 35 U.S.C. §1.132, executed by the named inventors of the present application. As stated in the accompanied declarations, subject matter relating to purification of monomeric BMT proteins including MP52, which is disclosed but not claimed in Andou, was derived from the named inventors of the present application. Likewise, the subject matter relating to producing monomeric BMP proteins including MP52 having a cysteine mutated to prevent intermolecular disulfide bonds, which is

reversed phase HPLC, lanes 6-10 of Fig. 3) as proven by the sensitive Western Blot in Fig. 3.

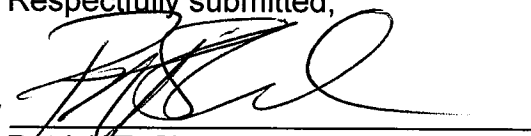
disclosed but not claimed in Hötten, was also derived from the named inventors of the present application. Therefore, the claimed invention is not an invention "by another" and these two patents cannot be applied to the claimed invention as prior art.

The Declaration effectively renders the current rejection moot and thus Applicants respectfully request withdrawal of this rejection.

In view of the foregoing, it is submitted that the present application is now in condition for allowance. Reconsideration and allowance of the pending claims are requested. The Director is authorized to charge any fees or overpayment to Deposit Account No. 02-2135.

Respectfully submitted,

By



Patrick T. Skacel
Attorney for Applicants
Registration No. 47,948
ROTHWELL, FIGG, ERNST & MANBECK, P.C.
Suite 800, 1425 K Street, N.W.
Washington, D.C. 20005
Telephone: (202)783 6040
Facsimile: (202)783-6031